

CLAIMS

What is claimed is:

1. A method for administering a therapeutic virus to a subject in one or more cycles, wherein at least one cycle comprises administering sequentially two or more desensitization doses of the virus followed by administering one or more escalated doses of the virus, wherein:
 - the virus is a negative-stranded RNA virus;
 - the amount of the virus in the second and any subsequent desensitization dose is not less than the amount of the virus in the preceding desensitization dose; and
 - the amount of the virus in each of the one or more escalated doses is higher than the amount of virus in each of the desensitization doses.
2. The method of claim 1, wherein the virus is a replication-competent oncolytic virus.
3. The method of claim 2, wherein the oncolytic virus is a Paramyxovirus.
4. The method of claim 3, wherein the Paramyxovirus is a Newcastle Disease Virus.
5. The method of claim 4, wherein the virus is a mesogenic strain of Newcastle Disease Virus.
6. The method of claim 5, wherein the first desensitizing dose is at least 1×10^8 PFU per square meter of patient surface area.
7. The method of claim 6, wherein the first desensitizing dose is at least 3×10^8 PFU per square meter of patient surface area.

8. The method of claim 7, wherein the first desensitizing dose is at least 1×10^9 PFU per square meter of patient surface area.
9. The method of claim 5, wherein the second desensitizing dose is at least 3×10^9 PFU per square meter of patient surface area.
10. The method of claim 9, wherein the second desensitizing dose is at least 5.9×10^9 PFU per square meter of patient surface area.
11. The method of claim 10, wherein the second desensitizing dose is at least 1.2×10^{10} PFU per square meter of patient surface area.
12. The method of claim 5, wherein the escalated doses are each at least 3×10^9 PFU per square meter of patient surface area.
13. The method of claim 12, wherein the escalated doses are at least 5.9×10^9 PFU per square meter of patient surface area.
14. The method of claim 13, wherein the escalated doses are at least 1.2×10^{10} PFU per square meter of patient surface area.
15. The method of claim 14, wherein the escalated doses are at least 2.4×10^{10} PFU per square meter of patient surface area.
16. The method of claim 15, wherein the escalated doses are at least 4.8×10^{10} PFU per square meter of patient surface area.
17. The method of claim 16, wherein the escalated doses are at least 9.6×10^{10} PFU per square meter of patient surface area.

18. The method of claim 17, wherein the escalated doses are at least 1.2×10^{11} PFU per square meter of patient surface area.
19. The method of claim 18, wherein the escalated doses are at least 1.44×10^{11} PFU per square meter of patient surface area.
20. The method of claim 19, wherein the escalated doses are at least 1.96×10^{11} PFU per square meter of patient surface area.
21. The method of claim 5, wherein the number of desensitization doses administered is two.
22. The method of claim 5, wherein the number of desensitization doses administered is at least three.
23. The method of claim 22, wherein the third desensitization dose is at least 3×10^9 PFU per square meter of patient surface area.
24. The method of claim 23, wherein the third desensitization dose is at least 5.9×10^9 PFU per square meter of patient surface area.
25. The method of claim 24, wherein the third desensitization dose is at least 1.2×10^{10} PFU per square meter of patient surface area.
26. The method of claim 5, wherein the first desensitization dose:
 - is administered over an administration time period of up to 24 hours; and
 - is administered at a rate of up to 3.0×10^9 PFU per square meter of patient surface area in any ten minute sampling time period within the administration time period.

27. The method of claim 26, wherein the rate is up to 6.7×10^8 PFU per square meter of patient surface area in any ten minute sampling time period within the administration time period.

28. The method of claim 27, wherein the rate is up to 3.3×10^8 PFU per square meter of patient surface area in any ten minute sampling time period within the administration time period.

29. The method of claim 5, wherein one or more doses selected from the second desensitization dose, any subsequent desensitization dose and an escalated dose:
is administered over an administration time period of less than 24 hours; and
is administered at a rate of up to 5.0×10^{10} PFU per square meter of patient surface area in any ten minute sampling time period within the administration time period.

30. The method of claim 29, wherein the rate is up to 2.0×10^{10} PFU per square meter of patient surface area in any ten minute sampling time period within the administration time period.

31. The method of claim 2, wherein the oncolytic virus is a Rhabdovirus.

32. The method of claim 31, wherein the Rhabdovirus is a Vesicular Stomatitis Virus.

33. The method of claim 1, wherein the amount of the virus in the second and any subsequent desensitization dose is greater than the amount of the virus in the preceding desensitization dose.

34. The method of claim 1, wherein the virus is administered to the subject intravenously.

35. The method of claim 1, wherein the subject is a human subject.

36. The method of claim 1, wherein the subject is a non-human mammal.
37. A method for administering a dose of a therapeutic virus to a subject, wherein:
the virus is a negative-stranded RNA virus;
the dose is the first dose in a cycle comprising one or more doses of the virus;
the dose is administered over an administration time period of up to 24 hours; and
the dose is administered at a rate of up to 3.0×10^9 PFU per square meter of patient surface area in any ten minute sampling time period within the administration time period.
38. The method of claim 37, wherein the rate is up to 6.7×10^8 PFU per square meter of patient surface area in any ten minute sampling time period within the administration time period.
39. The method of claim 38, wherein the rate is up to 3.3×10^8 PFU per square meter of patient surface area in any ten minute sampling time period within the administration time period.
40. The method of claim 37, wherein the virus is a replication-competent oncolytic virus.
41. The method of claim 40, wherein the oncolytic virus is a Paramyxovirus.
42. The method of claim 41, wherein the Paramyxovirus is a Newcastle Disease Virus.
43. The method of claim 42, wherein the virus is a mesogenic strain of Newcastle Disease Virus.

44. The method of claim 43, wherein the first dose is at least 1×10^8 PFU per square meter of patient surface area.
45. The method of claim 44, wherein the first dose is at least 3×10^8 PFU per square meter of patient surface area.
46. The method of claim 45, wherein the first dose is at least 1×10^9 PFU per square meter of patient surface area.
47. The method of claim 37, wherein the virus is administered to the subject intravenously.
48. The method of claim 37, wherein the subject is a human subject.
49. The method of claim 37, wherein the subject is a non-human mammal.
50. The method of claim 37, wherein the administration time period is at least 1 hour.
51. The method of claim 50, wherein the administration time period is at least 3 hours.
52. A method for administering a dose of a therapeutic virus to a subject, wherein:
 - the virus is a negative-stranded RNA virus;
 - the dose is the second or subsequent dose in a cycle comprising two or more doses of the virus;
 - the dose is administered over an administration time period of up to 24 hours; and
 - the dose is administered at a rate of up to 5.0×10^{10} PFU per square meter of patient surface area in any ten minute sampling time period within the administration time period.

53. The method of claim 52, wherein the rate is up to 2.0×10^{10} PFU per square meter of patient surface area in any ten minute sampling time period within the administration time period.
54. The method of claim 52, wherein the virus is a replication-competent oncolytic virus.
55. The method of claim 54, wherein the oncolytic virus is a Paramyxovirus.
56. The method of claim 55, wherein the Paramyxovirus is a Newcastle Disease Virus.
57. The method of claim 56, wherein the virus is a mesogenic strain of Newcastle Disease Virus.
58. The method of claim 57, wherein the second or subsequent dose is at least 3×10^9 PFU per square meter of patient surface area.
59. The method of claim 58, wherein second or subsequent dose is at least 5.9×10^9 PFU per square meter of patient surface area.
60. The method of claim 59, wherein the second or subsequent dose is at least 1.2×10^{10} PFU per square meter of patient surface area.
61. The method of claim 60, wherein the second or subsequent dose is at least 2.4×10^{10} PFU per square meter of patient surface area.
62. The method of claim 61, wherein the second or subsequent dose is at least 4.8×10^{10} PFU per square meter of patient surface area.

63. The method of claim 62, wherein the second or subsequent dose is at least 9.6×10^{10} PFU per square meter of patient surface area.
64. The method of claim 63, wherein the second or subsequent dose is at least 1.2×10^{11} PFU per square meter of patient surface area.
65. The method of claim 64, wherein the second or subsequent dose is at least 1.44×10^{11} PFU per square meter of patient surface area.
66. The method of claim 65, wherein the second or subsequent dose is at least 1.96×10^{11} PFU per square meter of patient surface area.
67. The method of claim 52, wherein the virus is administered to the subject intravenously.
68. The method of claim 52, wherein the subject is a human subject.
69. The method of claim 52, wherein the subject is a non-human mammal.
70. The method of claim 52, wherein the administration time period is at least 1 hour.
71. The method of claim 70, wherein the administration time period is at least 3 hours.